Claims

What is claimed is:

1. A Factor VII or Factor IX polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue 11 or 29.

2. The polypeptide of claim 1, wherein said polypeptide comprises Factor VII or Factor VIIa.

3. The polypeptide of claim 2, wherein a glutamine, a glutamic acid, an aspartic acid, or an asparagine residue is substituted at residue 11.

4. The polypeptide of claim 3, wherein a glutamine residue is substituted at residue 11.

5. The polypeptide of claim 2, wherein a glutamic acid or a phenylalanine residue is substituted at residue 29.

6. The polypeptide of claim 3, wherein a glutamic acid or a phenylalanine is substituted at residue 29.

7. The polypeptide of claim 2, wherein said modified domain further comprises an amino acid substitution at residue 33.

8. The polypeptide of claim 7, wherein a glutamic acid or an aspartic acid is substituted at residue 33.

9. The polypeptide of claim 3, wherein said modified GLA domain further comprises a substitution of a glutamic acid or an aspartic acid at residue 33.

10. The polypeptide of claim 5, wherein said modified GLA domain further comprises a substitution of a glutamic acid or a aspartic acid at residue 33.

11. The polypeptide of claim 3, wherein said modified GLA domain further comprises a substitution of a glutamic acid or a phenylalanine at residue 29.

12. The polypeptide of claim 11, wherein said modified GLA domain comprises a glutamic acid or an aspartic acid residue at amino acid 33.

13. The polypeptide of claim 9, wherein said modified GLA domain comprises a glutamine residue at amino acid 11 and a glutamic acid residue at amino acid 33.

14. The polypeptide of claim 11, wherein said modified GLA domain comprises a substitution of a glutamine at residue 11 and a phenylalanine at residue 29.

15. The polypeptide of claim 1, wherein said polypeptide comprises Factor IX or Factor IXa.

16. The polypeptide of claim 2, wherein said polypeptide comprises active-site modified Factor VIIa.

17. A Factor VII or Factor IX polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising an aspartic acid residue at amino acid 33.

18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an amount of a Factor VII or Factor IX polypeptide effective to increase clot formation in a mammal, wherein said Factor VII or Factor IX polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue 11 or 29.

19. The pharmaceutical composition of claim 18, wherein said pharmaceutical composition further comprises soluble tissue factor.

20. A method of increasing clot formation in a mammal comprising administering an amount of a Factor VII or Factor IX polypeptide effective to increase clot formation in said mammal, wherein said Factor VII or Factor IX polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue 11 or 29.

21. A method for treating a bleeding disorder in a patient, said method comprising administering the pharmaceutical composition of claim 18 to said patient.

22. An isolated nucleic acid molecule, said molecule comprising a nucleic acid sequence encoding the polypeptide of claim 1.

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